REMARKS

In the Office Action mailed July 22, 2008, claims 35, 51-52, 54-61, 65, 75-82 were pending for consideration. All of the claims were rejected under 35 U.S.C. 103(a) which rejection is addressed in below.

By the present amendment, claims 39, 59, and 60 have each been amended to include the limitation delete that less than 50% of the cilostazol in the formulation is released within the first two hours and to reincorporate the previously removed tocopherol polyethyleneglyocol succinate compounds. Support for the release rate amendment can be found *inter alia* in the FIGS 2 and 4 of the originally filed application each of which correspond to formulations presented in Example 2 and Example 6 respectively. Applicants submit that the described formulations and the associated data presented in the FIGS 2 and 4 provide ample support for the scope of the presently amended claims. Applicants submit that no new matter has been added through this or any previous amendment of the claims.

It is to be understood that all amendments have been made solely for the purpose of expediting prosecution of the present application, and without conceding the correctness of the Examiner's rejection. Accordingly, claims 35, 51-52, 55, 57-61, 65, 75, 76, 78, and 80-82 are pending for consideration in the present application. Applicants respectfully submit that the present claims are allowable over the cited reference, and that the rejection in view thereof is now moot.

35 U.S.C. § 103 Rejections:

The Examiner has rejected each of the pending claims under 35 U.S.C. § 103(a) as being allegedly unpatentable over the U.S. Patent No. 5,891,469 to Amselem et al. (hereinafter

"Amselem") patent in view of The Merck Index (Eleventh Edition, Monograph 2277, 1989; pages 353-354). Applicants have amended each of claims 35, 59, and 60 to include the limitation wherein less than 50% of the cilostazol is released within the first two hours and have further reintroduced the tocopherol polyethyleneglycol succinate compounds present in the original claim but deleted in the previous amendment.

Amselem teaches a solid dry coprecipitate of lipophilic active ingredients and tocopherol polyethyleneglycol succinate (TPGS) which is formed when the active ingredient is co-melted with the TPGS. The coprecipitates can be incorporated into oral dosage forms to provide improved release of the active agent in vitro and enhanced oral bioavailability. However, Amselem does not teach delivering cilostazol, or any other active agent, over an extended period of time or with the release characteristics required by the presently pending claims. The Examiner has asserted that because Amselem showed various formulations which showed release of an active agent gradually increasing over the course of 120 minutes, such release constituted extended release over a period of time of 2 hours. Without conceding the correctness of such an assertion and merely to advance prosecution of the claims, Applicants have amended the claims to require that less than 50% of the cilostazol in the formulation be released within the first two hours.

Each of the compositions shown in Amselem provides a release profile which would be considered by those of ordinary skill in the art to be an "immediate release" profile. Such profiles clearly show that well in excess of 50% of the active agents in the various formulations are released within the first two hours. In fact, the immediate release profiles shown in Amselem's FIG 1 all show in excess of 50% release of the active agent within about the first 10 minutes. Amselem even heralds the rapid release of provided by its formulations. For Example,

in describing the release profiles of the formulations shown in FIG 1, Amselem states: "[d]epending on the specific composition of the formulation, very good Dexanabinol release (from 60-95%) was obtained – mainly during the initial 10-20 minutes. (emphasis added) (col. 9, lines 59-61) Another example of Amselem hailing the rapid release characteristics of its composition is found in Example 7, where a marketed (preexisting) product was compared to the claimed composition by stating "[t]he release of CoQ10 from the marketed product was very low compared to a very quick and significant release from the powdered TPGS/PVP coprecipitate formulation." (emphasis added) (col. 12, lines 24-26). Applicants assert that such passages as well as the figures of Amselem are unambiguous in their teachings that the compositions taught by Amselem have release characteristics which are "very quick" or immediate. Accordingly, as discussed with the Examiner in the telephonic interview of October 30, 2008, Applicants assert that Amselem fails to teach or suggest of composition which provides release over an extended period of time of 2 to 24 hours and which releases less than 50% of the cilostazol in the formulation within the first two hours. Such elements are also not taught in the secondary references of the rejection.

Further, Applicants assert that, upon review of the teachings of Amselm (e.g. the above passages), one of ordinary skill in the art would be disincentivised from using the formulations taught by Amselem to formulate a product or composition which had the presently claimed release characteristics, namely being released over an extended period of time of 2-24 hours and releasing less than 50% of the cilostazol within the first 2 hours. In other words, Applicants assert that Amselem's teachings effectively teach away from the use of the taught compositions in formulating products having the presently extended release characteristics.

As the Applicant has raised the issue of teaching away, the Applicant would like to review the current case law regarding teaching away for the Examiner's convenience. The Court of Appeals for the Federal Circuit has clearly stated that "an applicant may rebut a prima facie case of obviousness by showing that the prior art teaches away from the claimed invention in any material respect." In re Petersen, 315 F.3d 1325, 1331 (Fed. Cir. 2003). The Court has also stated that "[w]e have noted elsewhere, as a 'useful general rule,' that references that teach away cannot serve to create a prima facie case of obviousness." (emphasis added) McGinley v. Franklin Sports, Inc., 262 F.3d 1339, 1354 (Fed. Cir. 2001). In identifying the appropriate standard for teaching away, the Court has further stated:

> "A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be **discouraged from following the path set out in the reference**, or would be led in a direction divergent from the path that was taken by the applicant. The degree of teaching away will of course depend on the particular facts; in general, **a reference will teach away if it suggests** that the **line of development** flowing from the reference's disclosure **is unlikely to be productive** of the result sought by the applicant." (emphasis added) In re Gurley, 27 F.3d 551, 553 (Fed. Cir. 1994).

Clearly in the present case, a person of ordinary skill in the art would be disincentivised (i.e. led away) from preparing a formulation which was intended to provide release over an extended period of time of 2 to 24 hours and which would release less than 50% of the cilostazol within the first two hours.

In light of the above arguments, Applicants submit that the combination of Amselem and Merck fails to present a *prima facie* case of obviousness in that the references taken together fail to teach each and every element of the pending claims, namely a composition which includes compositions which have at least one of the presently claimed solubilizers and at least one of the presently claimed release modulators which provides extended release over a period of time of 2 to 24 hours and which releases less than 50% of the cilostazol in the first two hours. Further

such, Applicants assert that the combination of references fails to render the presently pending claims obvious because one skilled in the art would be disincentivised from making the presently claimed compositions using the compositions in Amselem due to their characteristic of providing rapid release of the active agent. Accordingly, it is respectfully requested that the rejection be withdrawn and the claims be allowed.

CONCLUSION

In view of the foregoing, the Applicants believe that claims 35, 51-52, 55, 57-61, 65, 75, 76, 78, and 80-82 present allowable subject matter and the prompt allowance thereof is requested. If any impediment to the allowance of these claims remains after consideration of the present amendment and above remarks, and such impediment could be removed during a telephone interview, the Examiner is invited to telephone the undersigned attorney, so that such issues may be resolved as expeditiously as possible.

Please charge any additional fees except for Issue Fee or credit any overpayment to Deposit Account No. 20-0100.

Dated this 14th day of November, 2008.

Respectfully submitted,

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